HIGH PRODUCTION VOLUME (HPV)

CHALLENGE PROGRAM

FINAL SUBMISSION

For

Methylcyclopentadienyl Manganese Tricarbonyl
(MMT®)

Prepared by
The American Chemistry Council
Petroleum Additives Panel
Health, Environmental and Regulatory Task Group

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LIST OF MEMBER COMPANIES IN THE
HEALTH, ENVIRONMENTAL AND REGULATORY TASK GROUP

The Health, Environmental, and Regulatory Task Group (HERTG) of the American Chemistry Council Petroleum Additives Panel include the following member companies:

Afton Chemical Corporation (formerly Ethyl Corporation)

Chevron Oronite Company, LLC

Infineum

The Lubrizol Corporation

1.0 INTRODUCTION

In March 1999, the American Chemistry Council Petroleum Additives Panel Health, Environmental and Regulatory Task Group (HERTG), and its participating member companies committed to participate in the Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program for certain chemicals. The test plan followed up on that commitment. Specifically, the test plan set forth how the HERTG intended to address the relevant endpoints for the following substance - Methylcyclopentadienyl Manganese Tricarbonyl (CAS No.: 12108-13-3)

In preparing the test plan the following steps were undertaken:

Step 1: A review of the literature and confidential company data was conducted on the physicochemical properties, mammalian toxicity endpoints, and environmental fate and effects for Methylcyclopentadienyl Manganese Tricarbonyl (CAS No.: 12108-13-3) using its CAS number, CAS name, and synonyms. Searches included the following sources: MEDLINE, BIOSIS, CANCERLIT, CAPLUS, CHEMLIST, EMBASE, HSDB, RTECS, EMIC, and TOXLINE databases; the TSCATS database for relevant unpublished studies on these chemicals; and standard handbooks and databases (e.g., Sax, CRC Handbook on Chemicals, IUCLID, Merck Index, and other references) for physicochemical properties.

Step 2: The compiled data was evaluated for adequacy in accordance with the EPA guidance documentation.

This final submission summarizes the results of the test plan.

2.0 GENERAL SUBSTANCE INFORMATION

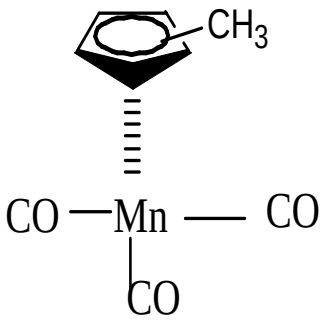
Methylcyclopentadienyl Manganese Tricarbonyl (MMT) is used as a petroleum additive in petroleum base stocks. The chemical name, CAS Registry Number, molecular weight and chemical structure for this substance are:

Chemical Name: Methylcyclopentadienyl Manganese Tricarbonyl (MMT)

Chemical Abstract Service Registry Number: 12108-13-3

Molecular Weight: 218.1 g/mol

Chemical Structure:



12108-13-3

3.0 EXPOSURE INFORMATION

3.1 Manufacture

Methylcyclopentadienyl Manganese Tricarbonyl (MMT) is manufactured at a plant that is under a toll manufacturing agreement with a member of the HERTG.

The manufacturing process entails the following. Under a nitrogen atmosphere, methylcyclopentadienyl dimer is added to a dispersion of sodium metal in diethylene glycol dimethyl ether. A constant elevated reaction temperature is maintained to yield sodium-methylcyclopentadienyl, which is an intermediate in the reaction process. Manganese chloride is then added to the stirred mixture containing the sodium – methylcyclopendienyl intermediate. An elevated temperature is maintained during the addition. Upon completion, the reaction gives bis (methylcyclopentadienyl)manganese, the second intermediate of the reaction process. The reaction vessel is then pressurized with carbon monoxide. The addition of carbon monoxide results in MMT which is separated from the reaction mixture via vacuum distillation.

3.2 Use

MMT is a fuel additive that boosts gasoline octane and improves combustion. MMT also helps lower tailpipe emissions of NOx and reduce refinery emissions of nitrous oxide. Both emissions are so called “green house gases” that may be linked to global warming.

4.0 PHYSICOCHEMICAL PROPERTIES

4.1 Boiling Point and Vapor Pressure

MMT has a boiling point of 231.67 ^{o}C and a vapor pressure of 7.3 mm Hg at 100 ^{o}C.

4.2 Water Solubility and Octanol-Water Partition Coefficient

The water solubility at 25ºC is 29 mg/L. The octanol/water partition coefficient Log Kow=3.7. MMT is a liquid and, therefore, the melting point is not applicable.

5.0 ENVIRONMENTAL FATE DATA

5.1 Biodegradability

An OECD 301 D was conducted on MMT which showed that the chemical is not readily biodegradeable. Gas Liquid Chromatography results of day 0 test material analysis indicated that approximately 60% of the applied test material dose was in solution (2.4 mg/L), while the other 40% did not dissolve. Study results were corrected for the actual amount of test material in solution. More than 90% of the positive control applied dose was biodegraded in the 28-day test period. This verified that the microbial inoculum was viable and active. Approximately 46% of the test material in solution was biodegraded. Biodegradation appeared to have ceased between day 15 and 28. Since the measured BOD was not greater than 60% of the TOD, the test material was not readily biodegradable under these test conditions. The uninoculated and inoculated blanks met the appropriate acceptance criteria.

5.2 Hydrolysis

In the absence of light, MMT undergoes a very slow hydrolysis with a half-life range for both anaerobic and aerobic conditions of 0.2 to 1.5 years at 25° C.

5.3 Photodegradation

Photolysis of MMT in distilled water is quite rapid. The disappearance of the test material followed first order kinetics, with a calculated half-life of 0.93 minutes. The rate constant was 0.74 ± 0.01 min^{-1}. Reaction products were methylcyclopentadiene, cyclopentadiene and carbon monoxide and a manganese carbonyl that readily oxidized to trimanganese tetroxide.

5.4 Fugacity Modeling

In a May 20, 2004 letter[1], EPA recommended use of the EQC Level III fugacity model rather than EQC Level I that was originally proposed in the test plan. A key difference between Levels I and III is that Level I assumes a fixed quantity of a chemical in a closed environment has reached an equilibrium state, while Level III assumes that only a steady state of equal inputs and outputs to a system has been achieved without obtaining thermodynamic equilibrium. Level III modeling, according to EPA is “more realistic

[1]USEPA Comments on Chemical RTK HPV Challenge Submission: Methylcyclopentadienyl Manganese Tricarbonyl (MMT), posted at http://www.epa.gov/chemrtk/mthmntri/c14889ct.htm

where releases are relatively constant over time."[2, 3] Whether Level I or III modeling is more appropriate is secondary to the fundamental question: will fugacity modeling yield meaningful information that affords a more accurate estimate of MMT's transport and distribution in the environment? Considering EPA's purpose in requesting fugacity modeling in the HPV Challenge Program, considering what is already known regarding MMT's physico-chemical properties, and considering the model outputs, fugacity modeling to estimate MMT movement in environmental compartments will provide no meaningful information to materially change what is already known regarding MMT's behavior in the environment.

EPA's interest in requesting fugacity modeling was two-fold.[4] First, the Agency desired a method to estimate overall persistence, as a means of implementing efforts to control persistent, bioaccumulative, and toxic (PBT) chemicals. Second, EPA was interested in determining a chemical's potential for engaging in long-range transport (LRT). Neither of these reasons for requesting fugacity modeling is applicable to MMT. Regarding persistence and PBT issues, MMT contains Mn, and as a metal, of course, it is persistent. The Agency is in the process of reviewing the application of PBT criteria to metals in general.[5] Further, Mn is the 12th most abundant metal and, unlike Pb or Hg, it is essential for both animal and plant health.[6] Therefore, concerning the manganese portion of MMT, fugacity modeling will not provide relevant information regarding PBT issues. For MMT (the compound itself), the physico-chemical data already available is sufficient to make predictions regarding persistence without resorting to modeling. And, LRT, EPA's second reason for an in fugacity modeling, is not issue with MMT. The compound undergoes rapid photo-degradation that precludes LRT. Therefore, EPA's two reasons for requesting fugacity modeling do not apply to MMT.

As mentioned above, MMT physico-chemical properties are sufficient to make fugacity estimates without the need for modeling. The compound's rapid photo-degradation indicates very little apportionment to air. Its Log K_{ow} allows accurate estimates of MMT's behavior in water, including groundwater. The research already conducted in sediments provides data on aquatic systems.[7] Therefore, without modeling, fugacity estimates for MMT can be made.

Fugacity modeling is appropriate for a new chemical, where experience of having the chemical in commerce is limited. In the case of a new chemical having an estimate of

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[2] Canadian Environmental Modelling Centre, Level I Model, Vers. 2.11, August 1999, posted at http://www.trentu.ca/cemc/models/VBL1.html.

[3] Recommendations for Estimating Transport Between Environmental Compartment (Fugacity) for Existing Chemicals, including HPV chemicals, posted at http://www.epa.gov/opptintr/exposure/docs/eqchpv.html.

[4] *ibid*.

[5] USEPA, "Review of EPA Draft Framework for Inorganic Metals Risk Assessment," A Report by the Science Advisory Board Metals Risk Assessment Framework Review Panel, 3/29/05 – draft, posted at http://www.epa.gov/science1/pdf/metals_report_03-29-05_draft.pdf.

[6] Morgan, J., "Manganese in Natural Waters and Earth's Crust: It's Availability to Organisms," in Manganese a Comprehensive Review 2000; and ATSDR, Toxicological Profile for Manganese (Update), 2000.

[7] Garrison, et al., "Environmental Fate of Methylcyclopentadienyl Manganese Tricarbonyl," Environ Toxicol Chem 1995, 14, 1859-1864.

distribution and transport could be quite helpful. MMT is an old chemical, having been on the market since the late 1950's. A wealth of experience regarding potential releases to the environment is available. For example, controlled studies of partitioning of MMT in clay, sandy soil, wet sandy soil, and other media have been done.[8] In light of these experimental data, fugacity modeling is redundant and provides less information than is already available.

6.0 ECOTOXICOLOGY DATA

6.1 Aquatic Ecotoxicity Testing

The proposed testing of MMT for acute toxicity to fish and acute toxicity to algae using the OECD recommended testing guidelines will not yield meaningful results. Substitution of non-OECD test procedures may not be as reflective of conditions found in naturally-occurring aquatic environments and certainly the meaning and significance of non-OECD test results will not be as easily communicated or grasped by the global regulatory community, as the more familiar standard OECD testing guidelines. Further, sufficient information regarding MMT's behavior in aquatic environments already exists. For these reasons, no additional testing of MMT for acute toxicity to fish, daphnia and algae is warranted. The discussion below provides details and references in support of this position.

With a density of 1.38 g/L, MMT is heavier than water and, if spilled onto surface water, the compound sinks to the bottom. Once on the bottom, MMT absorbs onto sediment due to its hydrophobic character, as indicated by an octanol-water partition coefficient of 3.7. In the absence of light, MMT undergoes a very slow hydrolysis with a half-life range for both anaerobic and aerobic conditions of 0.2 to 1.5 years at 25° C. However, photolysis of MMT in distilled water is quite rapid as indicated by a half-life of less than 1 minute. Therefore, if light does not penetrate to the bottom of the water column, MMT absorbed onto sediment can persist and will equilibrate with the surrounding water according to its octanol-water partition coefficient.[9] The concentration of MMT under these conditions will be very low and most likely incapable of producing an acute toxic reaction in fish or free-floating algae. Considering MMT's partitioning into aqueous compartments and given its propensity to undergo rapid photolysis in the water column itself, standard acute toxicity tests in fish, daphnia and algae will not provide meaningful data.

[8] Internal Afton Chemical reports available upon request.
[9] Garrison et al., 1995; see fn. 7.

6.1.2 Acute Toxicity in Fish

OECD test guideline 203 applies to testing of substances for acute toxicity in fish.[10] Guideline 203 requires that "there must be evidence that the concentration of the substance being tested has been satisfactorily maintained, and preferably it should be at least 80 per cent of the nominal concentration." Guideline 203 also requires that the fish be exposed to light for a period of 12 to 16 hours per day. Under these test conditions, the concentration of MMT cannot be satisfactorily maintained due to rapid photolysis of the compound. This OECD testing guideline is not recommended for MMT. Further, the value of any acute toxicity testing in fish is questionable due not only to photolysis of the compound, but also to MMT's other properties such as density and octanol-water partition coefficient. The likelihood of fish being exposed to acutely toxic concentrations of MMT in naturally-occurring aquatic environments is remote.

6.1.3 Acute Toxicity in Algae

OECD test guideline 201 applies to testing of substances for acute toxicity in algae.[11] Similar to the 203 procedure for fish, guideline 201 requires the algae to have "continuous uniform illumination." Obviously, under these conditions MMT will undergo photolysis, thus precluding maintaining adequate concentrations of the compound that are in contact with the algae. Guideline 201 also requires the algae containing medium to contain $MnCl_2$ at a concentration of 0.415 mg/L, as a nutrient. The Mn-containing product of MMT photolysis is trimanganese tetraoxide, which itself might function as a nutrient for algae. These MMT properties indicate the compound does not pose a reasonable risk of acute toxicity to algae.

6.1.4 Acute Toxicity to Daphnia

OECD test guideline 202 applies to testing of substances for acute toxicity in daphnia.[12] Guideline 202 also requires that the fish be exposed to light for a period of 16 hours per day. Under these test conditions, the concentration of MMT cannot be satisfactorily maintained due to rapid photolysis of the compound. This OECD testing guideline is not recommended for MMT. Further, the value of any acute toxicity testing in daphnia is questionable due not only to photolysis of the compound, but also to MMT's other properties such as density and octanol-water partition coefficient. The likelihood of daphnia being exposed to acutely toxic concentrations of MMT in naturally-occurring aquatic environments is remote.

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[10] OECD Guideline for Testing of Chemicals, 203, "Fish, Acute Toxicity Test," adopted by the Council on July 17, 1992.

[11] OECD Guideline for Testing of Chemicals, 201, "Algae, Growth Inhibition Test," adopted by the Council on June 7, 1984.

[12] OECD Guideline for Testing of Chemicals, 202, "Daphnia, Acute Toxicity Test," adopted by the Council on June 7, 1984.

7.0 MAMMALIAN TOXICOLOGY DATA

7.1 Acute Mammalian Toxicity

7.1.1 Acute Oral Toxicity

LD50 (rat): 58 mg/kg (males and females) (37.4-89.9 mg/kg)
LD50 (rat): 175 mg/kg (males and females) (148-207mg/kg)

7.1.2 Acute Inhalation Toxicity

LC50 (1 hour) 0.247 mg/L (males) (95% confidence limits 0.229-0.271 mg/L)
LC50 (4 hour) 0.076 mg/L (males) (95% confidence limits 0.067-0.087 mg/L)

7.1.3 Acute Dermal Toxicity

LD50 (rabbit) = 140 mg/kg (122-159 mg/kg)
LD50 (rabbit) = 795 mg/kg (568-1113 mg/kg)
LD50 (rabbit) = 420 mg/kg (170-670 mg/kg)
LD50 (rabbit) = 196.7 mg/kg $\pm$ 37.46

7.2 Genetic Toxicity

7.2.1 Bacterial Reverse Mutation Assay

The test substance was not mutagenic in this assay with or without metabolic activation.

7.2.2 In Vitro Chromosomal Aberration Assay in CHO Cells

An increase in the percentage of cells that contained chromosome aberrations was observed in the presence of metabolic activation, but not in the absence of metabolic activation.

7.2.3 Mammalian Erythrocyte Micronucleus Test

Two studies were performed, both of which showed no elevation in micronuclei, thus no genotoxicity.

7.3 Repeated-dose, Reproductive and Developmental Toxicity

7.3.1 Repeated-dose Toxicity

A 14 week inhalation study was conducted in rats, mice, and primates at dose levels of 0.3, 3.5, 30.2 ug/L. Significant toxicity was observed at the mid and high exposure levels.

Based on the results of this study, the Study Director concluded that the mouse was the species most sensitive to vapor inhalation exposure to this test material followed by the rat and monkey respectively. In addition female rodents appeared to be more sensitive then male rodents.

A NOAEL of 0.3 ug/L was selected based on the increased blood urea nitrogen levels observed in rats at all exposure levels. This study satisfies the repeat dose toxicity endpoint for HPV purposes.

7.3.2 Developmental Toxicity

Pregnant female rats were dosed on gestation days 6-15 with 0, 2.0, 4.5, 6.5, or 9.0 mg/kg/day. Maternal toxicity was observed at the high dose level, 9 mg/kg, as evidenced by anogenital staining and maternal weight loss early in the treatment period. A slight reduction in mean fetal body weights and a slight to moderate reduction in mean maternal body weight over the entire gestation period were noted at all treatment dose levels. No significant developmental toxicity was observed.

The NOAEL for maternal effects was 6.5 mg/kg and the NOAEL for developmental effects was >9 mg/kg (the highest dose tested).

7.3.2 Reproductive Toxicity

No published or unpublished reproductive toxicity studies on MMT were located; however, the 14 week repeat exposure inhalation study conducted in rats, mice and primates discussed above (dose levels of 0.3, 3.5, 30.2 ug/L) included the microscopic evaluation of both male and female rat and mouse and male primate reproductive organs. No reproductive toxicity was observed at the high exposure level (30.2 ug/L) in any species. This study provides information on the reproductive toxicity endpoint MMT for HPV purposes.

Table 1

SUMMARY OF DATA

CAS No.: 12108-13-3	Study Results
Physical/Chemical Characteristics	
Melting Point	Liquid
Boiling Point	231.67 °C
Vapor Pressure	7.3 mm Hg at 100 °C
Water Solubility	29 mg/L
Partition Coefficient	3.7
Environmental Fate	
Biodegradation	Not readily biodegradeable
Hydrolysis	In the absence of light, half-life range for both anaerobic and aerobic conditions of 0.2 to 1.5 years at 25° C.
Photodegradation	Half-life in midday sunlight~1 minute
Fugacity	Not performed – environmental fate already understood
Ecotoxicity	
Acute Toxicity to Fish	Not performed – exposure very unlikely
Acute Toxicity to Invertebrates	Not performed – exposure very unlikely
Acute Toxicity to Algae	Not performed – exposure very unlikely
Mammalian Toxicity	
Acute Toxicity	Oral LD50: 58-175 mg/kg (rat) Dermal LD50: 140-795 mg/kg (rabbit) Inhalation 1 Hour LC50: 0.247 mg/L (rat) Inhalation 4 Hour LC50: 0.076 mg/L (rat)
Repeated Dose Toxicity	14 Week Inhalation NOAEL: 0.3 ug/L (rat)
Developmental Toxicity	NOAEL: 9 mg/kg/day (gestation days 6-15)
Reproductive Toxicity	14 Week Inhalation - NOAEL: 30.2 ug/L (for reproductive toxicity in mouse, rat, primate)
Genotoxicity	
Gene Mutation	Negative
Chromosomal Aberration	in vitro CHO without activation-positive; In vitro CHO with activation and in vivo in mouse-negative